IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Satish Mahadeorao Totey and Geeta Ravindran	Group Art Unit: 1647
Serial No.: 10/798,790	Examiner: Daniel C. Gamett
Filed: March 11, 2004	Atty. Dkt. No.: REL494/4-002US/58000
For: DERIVATION OF TERMINALLY DIFFERENTIATED DOPAMINERGIC NEURONS FROM HUMAN EMBRYONIC STEM CELLS	Confirmation No. 5605

CERTIFICATE OF MAILING

I certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to Mail Stop Fee Amendment, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 on the date below:

August 12, 2009 Margaret Sampson
Date Margaret Sampson

MAIL STOP AMENDMENT
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF GEETA RAVINDRAN UNDER 37 C.F.R. § 1.132

I, GEETA RAVINDRAN, HEREBY DECLARE AS FOLLOWS:

1. I, Geeta Ravindran, am a co-inventor of the subject matter disclosed and claimed in the above-referenced patent application. I am a Research Scientist in the Embryonic Stem Cell Group at Reliance Life Sciences Pvt. Ltd., which is the assignee of the above-referenced patent application. A brief copy of my *curriculum vitae* is attached hereto as **Exhibit A.**

2. I am a citizen of India residing at A-1/1104, Lok Gaurav, LBS Marg, Ghandi Nagar, Vikhroli (W), Mumbai, Maharashtra, 400 083, India.

3. I have become aware that Table 1 of the specification as originally filed contains certain clerical errors that were made during the preparation of Table 1. Therefore, I am providing herewith a revised version of Table 1, which corrects these errors (**Exhibit B**). In addition, I am providing a clean copy of revised Table 1 (**Exhibit C**).

4. The first row of Table 1, which includes the same culture conditions as the second row of Table 1 but a different percentage of TH positive cells, was left in Table 1 by mistake and has been removed. The second row of Table 1 has been clarified to indicate that this row represents results of cells that were not sorted. Additionally, the percentage of TH positive cells was reversed between the second and third row of Table 1. Both of these changes are supported by **[00120]** of the specification as originally filed, which details that "the percentage of sorted NCAM-positive cells expressing TH is about 60%," while "about 40% of the nestin-positive cells stained positively for TH." The third row of Table 1 has also been corrected to remove duplicate entries of Shh and FGF-8 in the second column, which were erroneously listed twice. Finally, a minor typographical error has been corrected in the fourth row of Table 1 in the percentage of TH positive cells.

5. I hereby declare that the errors contained in Table 1 of the specification as originally filed occurred without deceptive intent.

6. I hereby declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

4/5/2009
Date

Geeta S
Geeta Ravindran

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Exhibit A

Brief Resume:

I have completed my doctorate in Life Sciences (1995-1999) from Mumbai University, INDIA and have about 20 years research experience .The title of the thesis: 'Biochemical and immunological characterization of Cerebrospinal fluid (CSF) for the diagnosis of tuberculous meningitis (TBM).'

I am employed as Research Scientist, Embryonic stem cell group, Reliance Life Sciences Pvt. Ltd mainly involved in the generation of neurons and glial cells from embryonic stem cells and adult stem cells ; characterization of different neuronal phenotypes at cellular, molecular and functional levels followed by preclinical evaluation of the same in neurodegenerative disease models. Currently, I am on a sabbatical program at the National university of Singapore working on a project on the role specific nuclear factors on the directed differentiation of human embryonic stem cells

List of selected Publications/ Patents:

1) Shetty P, **Ravindran G** et al; manuscript accepted **(in Press)**
Clinical grade Mesenchymal stem cells transdifferentiated under xeno free conditions alleviates motor deficits in rat model of Parkinson's disease.

2) **Ravindran G,** Ramnath RL, Rao HS, Chandra V.
One year survival and significant reversal of motor deficits in parkinsonian rats transplanted with hESC derived dopaminergic neurons. Biochem Biophys Res Commun. 2008; 373 (2):258-64. Epub 2008 Jun 17.

3) Pal R*, **Ravindran G.***,
Assessment of pluripotency and multilineage differentiation potential of NTERA-2 cells as a model for studying human embryonic stem cells. Cell Prolif. (2006), 39 (6):585-98.
*Equal contribution

4) **Ravindran G,** Rao HS.
Enriched NCAM-positive cells form functional dopaminergic neurons in the rat model of Parkinson's disease. Stem Cells Dev. (2006) 15 (4):575-82.

Exhibit A

5) Mandal A, Tipnis S, Pal R, **Ravindran G**, Bose B, Patki A, Rao MS, Khanna A. Characterization and in vitro differentiation potential of a new human embryonic stem cell line, ReliCellhES1. Differentiation. (2006) 74 (2-3):81-90.

6) Dravida S, Pal R, Khanna A, Tipnis SP, **Ravindran G**, Khan F. The transdifferentiation potential of limbal fibroblast-like cells. Brain Res Dev Brain Res. (2005) 160 (2):239-51

7) Rajarshi Pal , Mandal A, **Ravindran G**, Khanna A Establishment, Characterization and Differentiation of Human Embryonic Stem Cells into Three Germ Layers, chapter in book **Human embryonic stem cells** ,Nova publications pp. 65-93 (2006)

8) **Geeta Ravindran**, Satish M Totey . Patent titled "Derivation of terminally differentiated Dopaminergic neurons from human Embryonic stem cell" granted in India, South Africa, Korea , Russia and Singapore.

9) Arundhati Mandal, Shabari Tipnis, Rajarshi Pal, **Geeta Ravindran**, Bipasha Bose, Jayant Kulkarni, Firdos A Khan, Ameet Patki, Aparna Khanna. Patent (provisional) titled "Establishment of a human embryonic stem cell using mammalian cells "has been filed in India.

10) **Geeta Ravindran** Harinarayana S Rao Patent titled "Dopaminergic neurons derived from corneal limbus methods of isolation and uses there of" has been filed in India and US.

111) Satish M Totey, Subhadra Kashyap, Firdos A Khan, Rajarshi Pal, Aparna Khanna, Shabri Tipnis, **Geeta Ravindran.** Patent titled Pluripotent Embryonic-Like Stem Cells Derived from Corneal Limbus, Methods of Isolation and Uses Thereof" has been filed in India and US.

Exhibit B

Table 1: Differentiation conditions for neuroprogenitor cells

Culture conditions for differentiation			
Days 1-4	Days 4-7	Days 8-50	TH positive cells (%)
~~Neurobasal medium, FCS, B27, IL-1β~~	~~Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF~~	~~Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin~~	~~65%~~
Neurobasal medium, FCS, B27, IL-1β Not sorted	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin	~~55%~~ 42%
Neurobasal medium, FCS, B27, IL-1β	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, ~~Shh, FGF-8,~~ BDNF, ascorbic acid	Neurobasal medium, Shh, FGF-8, FCS, B27, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin, ascorbic acid	~~42%~~ 55%
Neurobasal medium, FCS, B27, IL-1β	Neurobasal medium, Shh, FGF-8, FCS, B27, IL-1β, db-cAMP, GDNF, BDNF, N-acetyl cysteine	Neurobasal medium, Shh, FGF-8, FCS, B27, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin, N-acetyl cysteine	~~64%~~ 65%
Neurobasal medium, FCS, B27	Neurobasal medium, FCS, B27	Neurobasal medium, FCS, B27	20%

Exhibit C

Table 1: Differentiation conditions for neuroprogenitor cells

Culture conditions for differentiation			
Days 1-4	Days 4-7	Days 8-50	TH positive cells (%)
Neurobasal medium, FCS, B27, IL-1β Not sorted	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin	42%
Neurobasal medium, FCS, B27, IL-1β	Neurobasal medium, FCS, B27, Shh, FGF-8, IL-1β, db-cAMP, GDNF, BDNF, ascorbic acid	Neurobasal medium, Shh, FGF-8, FCS, B27, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin, ascorbic acid	55%
Neurobasal medium, FCS, B27, IL-1β	Neurobasal medium, Shh, FGF-8, FCS, B27, IL-1β, db-cAMP, GDNF, BDNF, N-acetyl cysteine	Neurobasal medium, Shh, FGF-8, FCS, B27, IL-1β, db-cAMP, GDNF, BDNF, TGF-β3, neurturin, N-acetyl cysteine	65%
Neurobasal medium, FCS, B27	Neurobasal medium, FCS, B27	Neurobasal medium, FCS, B27	20%